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10/727,510	12/05/2003	Kazuhisa Fukushima	032094	7859

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
06/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,510	FUKUSHIMA ET AL.	
	Examiner	Art Unit	
	JEANINE A. GOLDBERG	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5, 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 4, 2008. Currently, claims 2-5, 7 are pending.

2. All arguments have been thoroughly reviewed.

3. This action is FINAL.

Election/Restrictions

4. Applicant's election without traverse of Group 1, Claims 1-5 in the paper filed January 3, 2006 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Priority

5. This application claims priority to Japanese Appln No. 2002-353559, filed December 5, 2002.

It is noted that a translation of the foreign document has not been received.

Drawings

6. The drawings are acceptable.

New Matter

7. Newly Amended Claims 2-5, 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "beads each include one of a plurality of beads-ID and each of said beads-ID recognizing address linkers is specific to one of the plurality of beads-ID" are included. The amendment proposes that the new claim language clarifies the claimed subject matter and is supported on page 3, lines 23-25. However, the specification does not describe or discuss "beads each include one of a plurality of beads-ID and each of said beads-ID recognizing address linkers is specific to one of the plurality of beads-ID". The specification does not appear to suggest different beads-ID at any point of the 4 page specification. Instead the specification states "address linker 3 (address-judging antigen or address-judging antibody) for recognizing specific beads number ID is fixed on the surface of beads 1".

As seen in Figure 2, all of the beads-ID recognizing address linker (3) and the addressing probe proteins are illustrated identically. This description does not support beads-ID recognizing address linkers or beads-ID are specific to each of said beads. There is no discussion of specificity for the linkers or antigens.

The response provides a table and explanation on pages 4-5 of the response outlining a number of beads, different bead ID and beads ID recognizing address linker (3). The discussion does not point to any support in the specification for different beads ID or different beads ID recognizing address linker (3). This subject matter is new matter.

The response asserts that the recited subject matter relates to the specificity between the address linker 3 and the beads 1. This argument has been reviewed, and deemed not persuasive. While the specification discusses address linker 3 for recognizing specific beads number ID fixed on the surface of beads, this does not provide the necessary link to multiple linkers or recognizing bead number ID, as suggested by the response.

It is clear from applicants' later arguments with regard to the 103, that applicants are attempting to claim each antigen/antibody half must be specific to a single beads-ID and the number of configurations of antibody/antigen is the same as the number of sites. The specification fails to disclose any more than one configuration of antibody/antigen. The drawings illustrate all of the antibody and antigen configurations identical and there is no discussion in the specification of more than one configuration. The concept of "beads each include one of a plurality of beads-ID and each of said beads-ID recognizing address linkers is specific to one of the plurality of beads-ID" does not appear to be part of the originally filed invention. Therefore, "beads each include one of a plurality of beads-ID and each of said beads-ID recognizing address linkers is specific to one of the plurality of beads-ID" constitutes new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2, 4, 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramanian et al. (WO 00/06770, February 10, 2000) in view of Chee et al. (US 6,858,394, February 22, 2005).

Balasubramanian teaches arrayed biomolecules and their use in sequencing. Balasubramanian teaches a method of using an array which has a surface density which allow molecules to be individually resoled by optical microscopy. The method uses arrays which may be formed by simply immobilizing a mixture of molecules to a solid surface in such a way that provides sufficient separation between the molecules to allow each molecule to be resolved optically. The molecule is immobilized at one or more points by specific interaction with the surface (page 2, lines 29-32). Balasubramanian teaches that the arrayed molecules may be immobilized on a solid support via microspheres (page 3, lines 15-17). Balasubramanian teaches that the

microspheres are functionalized polystyrene latex microsphere (page 15)(limitations of Claim 4). Balasubramanian teaches that many thousands of reactions can be detected at the same time with no phasing problems (page 3, lines 32). The array of polynucleotides are contacted with a plurality of detectably-labeled fragments of an organism's genomic DNA under hybridizing conditions and detecting hybridization (page 4, lines 13-16). As seen in Figure 2, the immobilization of a polynucleotide to a solid surface via a microsphere is illustrated. Balasubramanian teaches that the arrays may comprise protein molecules immobilized on a solid surface, the protein molecules being conjugated with or otherwise bound to a short polynucleotide molecule may be interrogated, to address the array (page 6, lines 14-16). Balasubramanian teaches that the surface of the solid support may be coated with streptavidin or avidin and then a dilute solution of a biotinylated molecule is added at discrete sites on the surface (page 8, lines 1-4). If the molecule is a polynucleotide then immobilization may be via hybridization to a complementary nucleic acid molecule previously attached to a solid support (page 8). Balasubramanian teaches that the target molecules are immobilized onto the microspheres and the microspheres are immobilized in turn to a solid support to fix the target sample for microscope analysis (page 8). Thus, Balasubramanian teaches immobilizing primers on beads, contacting the beads with samples under hybridizing conditions to allow "self-sort" onto the bead. The beads are then in turn immobilized onto a solid support, array (page 8). Much like the schematic filed in the after-final amendment of 2/27/07, Figure 2 illustrates a protein interaction on the solid surface which immobilizes a bead with nucleic acid molecules which have been

hybridized with sample and labels. Balasubramanian teaches that "spatially addressable" is used to describe how different molecules may be identified on the basis of their position on an array (page 10, lines 15-20). Balasubramanian teaches that short sequences that a protein binds to may be used to find all the transcription-controlling proteins or cDNA (page 13)(limitations of Claim 5).

While Balasubramanian specifically teaches spatially addressing to determine and identify different molecules on the basis of their position on an array, Balasubramanian does not specifically teach spatially addressing the beads by an antigen-antibody reaction.

However, Chee teaches composite arrays using microspheres and methods for decoding microsphere array sensors. Chee teaches a method of decoding an array composition comprising providing an array composition and adding a plurality of decoding binding ligands to the composite array composition to identify the location of at least a plurality of the bioactive agents. Chee illustrates the addressability of specific substrates using analyte binding on a second substrate (see Figure 1F). Figure 1 F depicts the use of binding functionalities to "target" first substrates to locations on the second substrate (col. 2, lines 65-67). Chee teaches that biologically modified sties may be used to attach beads to the substrate. For example one partner is on the bead and the other is on the substrate. Particularly preferred in this embodiment are complementary nucleic acid strands and antigen/antibody pairs (col. 8, lines 45-50). Chee teaches that by using different populations with different binding partners, and a substrate comprising different array locations with spatially separated binding partners,

a composite array can be generated (col. 8, lines 59-61). The binding moieties may be used simply for attachment or for targeting the first substrate arrays to particular locations in or on the second substrate.

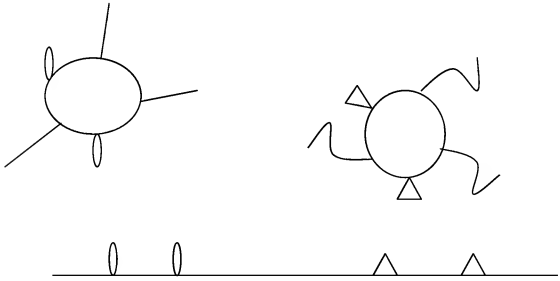
Chee teaches that the beads or microspheres may be plastics, ceramics, glass, polystyrene, methylstyrene, paramagnetic materials, for example (col. 9, lines 24-26)(limitations of Claim 4).

Chee teaches the target sequence may be a portion of a gene, a regulatory sequence, genomic DNA, cDNA, RNA (col. 13, lines 20-30)(limitations of Claim 5).

Therefore, it would have been prima facie obvious at the time the invention was made to have modified the protein interaction of Balasubramanian with the specific antibody/antigen interaction taught by Chee. Chee teaches that by using different populations with different binding partners, and a substrate comprising different array locations with spatially separated binding partners, a composite array can be generated. The antibody/antigen interaction is a simple detection means. Both Chee further teaches exemplary binding pairs are antibody/antigen pairs. The ordinary artisan would have been motivated to have modified the protein interactions of Balasubramanian with the simpler and highly specific binding pairs of Chee, namely antigen/antibody pairs. The ordinary artisan would have sorted and addressed the different populations of beads created by Balasubramanian using the methods of Chee to obtain specific sorting based upon interactions to identify the presence of analytes in a sample.

Response to Arguments

The response traverses the rejection. The response asserts that there would not have been any motivation to modify Balasubramanian as proposed by the Office Action. The response provides a drawing illustrating specific analytes for specific nucleic acids. This argument has been reviewed but is not deemed persuasive. While the drawing provides one possible embodiment where the bead comprises an analyte which binds to both the second substrate and the nucleic acid, the teachings of Chee illustrate that the nucleic acid may be bound covalently to the bead also. Chee specifically states that the surface chemistries for the microsphere include hydroxyl groups, amides, amino groups (see col. 15, lines 40-50). Thus, Chee suggests that the attached nucleic acids may not require the antigen/antibody half (see picture below). However, Chee does also suggest attachment with other chemistries as suggested by the response. Chee suggests both chemistries.



The response asserts that one having ordinary skill in the art would not have been prompted to modify Balasubramanian to include different antigen/antibody halves. This argument has been reviewed but is not persuasive. Balasubramanian specifically teaches spatially addressable methods (see page 10, lines 17--19). Chee teaches a specific example of a spatially addressable method. The ordinary artisan would have been motivated to have substituted the spatially addressable method of Balasubramanian with the spatially addressable method of Chee.

The response asserts that the proposed modification would drastically alter the method of Balasubramanian. The response asserts that Balasubramanian teaches the use of non-specific biotin and avidin. This argument has been reviewed but is not convincing. The ordinary artisan would have been motivated to have modified the non-specific manner exemplified by Balasubramanian with the specifically illustrated specific manner of Chee. Balasubramanian suggest spatially addressing the elements. Moreover, Chee specifically states that the formation of very high density arrays allows simultaneous analysis, i.e. parallel rather than serial processing, on a number of samples. Chee terms this forming an "array of arrays" (col. 3, lines 39-42). Chee further teaches very high numbers of assays can be run simultaneously (col. 3, lines 46-48). Thus, the ordinary artisan would have been motivated to have used the spatially addressable method of Chee to increase the throughput, and allow simultaneous analysis in parallel of larger number of analytes to be analyzed.

The response further asserts that the modification would drastically alter the preparation of the microspheres of Balasubramanian. This argument has been reviewed but is not persuasive. Chee illustrates the well known methods for attaching nucleic acids and antigen/antibody pairs to solid supports (see col. 15, lines 40-50), for example. The level of skill in the art for attaching nucleic acids and antigen/antibody pairs was extremely high. Nucleic acids have been attached to solid supports since the early 1990s, as have antigen/antibody pairs. It would have been well within the scope of the ordinary artisan to modify microspheres to attach alternative agents.

The response asserts that different types of beads, rather than a single bead, would be required which would dramatically increase the cost and complexity of the system of Balasubramanian. This argument has been reviewed but is not persuasive. The ordinary artisan would have been motivated to have generated a method which permitted the simultaneous analysis of multiple analytes including multiples beads for the benefits taught by Chee. Chee teaches that the simultaneous analysis of multiple analytes in parallel. The simultaneous analysis would save on reagents, time as well as provide for an automated system.

The response appears to argue again the probes of Balasubramanian would have to be prepared having different antigens/antibodies bound to each probe. This argument was addressed above. Chee teaches the biopolymers and beads-ID recognizing address linkers may be attached to the beads using any of a number of chemistries. The chemistries include amino, hydroxyl linkages for example. The chemistries may include antigen-antibody pairs also. The ordinary artisan would have

been motivated to have created linkages that were most convenient to their particular needs. As illustrated above, these linkages need not be antigen/antibody.

Thus for the reasons above and those already of record, the rejection is maintained.

10. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramanian et al. (WO 00/06770, February 10, 2000) in view of Chee et al. (US 6,858,394, February 22, 2005) as applied to Claims 2, 4, 5, 7 above and further in view of Collier et al. (US Pat. 5,985,548, November 1999).

Neither Balasubramanian nor Chee specifically teach a method of stirring beads.

However, Collier teaches beads and test mixtures are agitated to assure contact with the bead supports (see Example 2).

Therefore, it would have been prima facie obvious to the ordinary artisan at the time the invention was made to have added an agitation or stirring step to the bead method of Balasubramanian in view of Chee for the expected benefits taught by Collier. Collier specifically teaches the ordinary artisan would be motivated to agitate bead and test mixtures to assure contact with the bead supports. Thus, in order to ensure contact of the beads and mixtures, the ordinary artisan would have included an agitation step.

Response to Arguments

The response traverses the rejection. The response asserts that the claims are patentable at least due to its dependency on claim 7. This argument has been

considered but is not convincing for the reasons presented above. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

11. No claims allowable over the art.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

/Jeanine A Goldberg/
Primary Examiner, Art Unit 1634
June 12, 2008